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embodiments set forth in one Groups are separately patentable over the embodiments set forth in another Group, however, the search for art relevant to each of the embodiments would not create an undue burden on the Examiner.

Although they do not agree that the claims are properly divided into the four Groups set forth by the Examiner, Applicants have elected the claims of Group I solely to expedite prosecution and to obtain early issuance of a Notice of Allowance. Correspondingly, claims of the non-elected Groups are canceled.

Status of the Claims

Claims 1-75 are subject to restriction. Applicants have elected the claims of Group I (1-36), canceling those of Groups II-IV (37-75). Applicants have added new claims 76-93. Each of the new claims is directed to an embodiment of the probe set forth in the claims of Group I. Thus, the new claims are properly included in Group I and should not be subject to restriction or prompt the issuance of another Restriction Requirement. Claims 1, 3, 8, 9, and 18-32 are amended. Both the new claims and the amended claims are fully supported by the specification as filed. Therefore, no new matter is added.

The amendment of claims 1, and 8 by substituting the term "silicon oxide" for "glass" is supported at page 43, line 16 ("e.g., a probe surface comprised of silicon dioxide."). The replacement of "gas phase spectrometer" with "mass spectrometer" is supported at page 8, line 24.

The amendment to claim 3 is supported at page 15, lines 10-11. The dependence of claim 9 is changed from claim 5 to claim 1.

The transition term for claims 19-31 is amended from "are" to "comprise." Support for the amendments is found throughout the section describing exemplary binding functionalities on the hydrogels. The specific language is found at the following locations: claim 19—"comprise a carboxyl group" (p. 19, ln. 22); claim 20—"comprise a sulfonate group" (p. 19, ln. 27); claim 21—"comprise a phosphate group" (p. 19, ln. 30); claim 22—"comprise an ammonium group" (p. 20, ln. 1); claim 23—"comprise a hydrophilic

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group" (p. 20, ln. 13); claim 24—"comprise a hydrophobic group" (p. 20, ln. 21); claim 25—"comprise a metal chelating group" (p. 20, ln. 29); claim 26—"comprise a reactive group" (p. 21, ln. 1); claim 27—"comprise a thioether group" (p. 21, ln. 8); claim 28—"comprise a biotin group" (p. 21, ln. 12); claim 29—"comprise a boronate group" (p. 21, ln. 19); claim 30—"comprise a dye group" (p. 21, ln. 15); claim 31—"comprise a cholesterol group" (p. 21, ln. 22).

Claims 76 and 86 are supported by the specification as filed. See, for example, page 22, lines 1-3.

Claim 77 recites specific monomers from which the hydrogel is derived. Support for each of the recited monomers is found in originally filed claims 22, 19, and 25. Claim 78 sets forth hydrogels comprising cellulose or dextran. Support for these hydrogels is found at page 22, line 19.

Claim 79 sets forth a substrate that is substantially smooth. The claim is supported at page 15, line 28. Claim 80 sets forth a probe in which the hydrogel is about 1 micrometer thick. Support is found for this claim at page 18, lines 18-19. Claim 81 sets forth a substrate that comprises an insulating material. See, page 15, line 9. Claim 82 sets forth a probe having a substrate conditioned with a coupling agent through which the hydrogel adheres to the substrate. Support for claim 82 is found at page 17, line 12. Claim 83 sets forth a substrate on which the hydrogel is distributed in a plurality of discontinuous spots. See, claim 12 as filed. Support for claim 84, setting forth a silane coupling agent is found at page 17, line 12. Claim 85 sets forth an embodiment in which the hydrogel is attached to the surface in a series of discontinuous spots. Support for claim 85 is found in the specification. For example, at page 28, line 16 it is disclosed that the hydrogel can be "attached to a substrate in an array of pre-determined, addressable locations." Moreover claim 12 sets forth discontinuous spots. One of skill would understand that the discontinuous hydrogel spots adhering to the substrate were within the scope of the disclosure.

Claim 87 sets forth hydrogels that are cross-linked particles. Support for claim 87 is found at page 25, line 21 ("cross-linked polymers"). Claim 88 recites that the

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cross-linked particles comprise polystyrenes. See, page 25, line 22. Recitation of additional specific particle constituents in claim 89 is found at page 25, lines 21-23. Claim 90 sets forth that the particles are latex, which is supported at page 25, line 24. The plurality of particles is composed of particles having selected diameter range set forth in claims 91 and 92. Support for the ranges is found at page 25, lines 15-16.

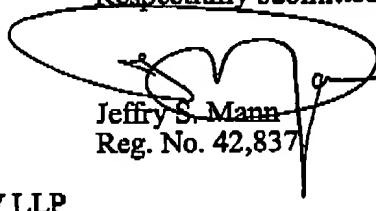
Claim 93 finds support in the specification at page 18, lines 15-16. The cited section recites an embodiment of the invention in which "the thickness of the coating on the substrate (e.g., glass coating) and the hydrogel material combined is at least about 1 micrometer thick." One of ordinary skill would understand the claimed range to include "about 1 micrometer thick." Thus, when the hydrogel and coating are about 1 micrometer thick, the hydrogel must be "less than about one micrometer thick."

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

WHAT IS CLAIMED IS:

- 1 1. (Once amended) A probe that is removably insertable into a [gas phase ion] mass spectrometer, the probe comprising a substrate having a surface coated with silicon oxide and a hydrogel material on the surface, wherein the hydrogel material is crosslinked and comprises binding functionalities for binding with an analyte detectable by the mass spectrometer.
- 1 2. (As filed) The probe of claim 1 wherein the substrate is in the form of a strip or a plate.
- 1 3. (Once amended) The probe of claim 1 wherein the substrate [is] comprises an electrically conducting material.
- 1 4. (As filed) The probe of claim 1 wherein the surface of the substrate is conditioned to adhere the hydrogel material.
- 1 5. (Cancel)
- 1 6. (As filed) The probe of claim 1 wherein the surface of the substrate is rough, porous or microporous.
- 1 7. (As filed) The probe of claim 1 wherein the hydrogel material is in situ polymerized on the surface of the substrate.
- 1 8. (Once amended) The probe of claim 1 wherein the [surface of the substrate is coated with a glass coating and wherein the] hydrogel material is in situ polymerized on the [glass] silicon oxide coating by depositing a solution comprising monomers onto the glass coating, wherein the monomers are pre-functionalized to provide binding functionalities.

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1 9. (Once amended) The probe of claim [5] 1 wherein the thickness of
2 the coating and the hydrogel material combined is at least about 1 micrometer.

1 10. (As filed) The probe of claim 1 wherein the hydrogel material is at
2 least about 1 micrometer thick.

1 11. (As filed) The probe of claim 1 wherein the hydrogel material is in
2 the form of a discontinuous pattern.

1 12. (Cancel)

1 13. (As filed) The probe of claim 1 wherein the hydrogel material is
2 continuous and has one or two-dimensional gradient of one or more of the binding
3 functionalities.

1 14. (As filed) The probe of claim 1 wherein a plurality of different
2 hydrogel materials comprising different binding functionalities are on the surface of the
3 substrate.

1 15. (As filed) The probe of claim 1 wherein the hydrogel material is a
2 homopolymer, a copolymer, or a blended polymer.

1 16. (As filed) The probe of claim 1 wherein the hydrogel material is
2 derived from substituted acrylamide monomers, substituted acrylate monomers, or
3 derivatives thereof.

1 17. (As filed) The probe of claim 1 wherein the binding functionalities
2 attract the analyte by salt-promoted interactions, hydrophilic interactions, electrostatic
3 interactions, coordinate interactions, covalent interactions, enzyme site interactions,
4 reversible covalent interactions, nonreversible covalent interactions, glycoprotein
5 interactions, biospecific interactions, or combinations thereof.

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1 18. (As filed) The probe of claim 1 wherein the binding functionalities
2 of the hydrogel material are selected from the group consisting of a carboxyl group, a
3 sulfonate group, a phosphate group, an ammonium group, a hydrophilic group, a
4 hydrophobic group, a reactive group, a metal chelating group, a thioether group, a biotin
5 group, a boronate group, a dye group, a cholesterol group, and derivatives thereof.

1 19. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a carboxyl group and the hydrogel material is derived from
3 monomers selected from the group consisting of (meth)acrylic acid, 2-carboxyethyl
4 acrylate, N-acryloyl-aminohexanoic acid, N-carboxymethylacrylamide, 2-
5 acrylamidoglycolic acid, and derivatives thereof.

1 20. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a sulfonate group and the hydrogel material is derived from
3 acrylamidomethyl-propane sulfonic acid monomers or derivatives thereof.

1 21. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a phosphate group and the hydrogel material is derived
3 from N-phosphoethyl acrylamide monomers or derivatives thereof.

1 22. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise an ammonium group and the hydrogel material is derived
3 from monomers selected from the group consisting of trimethylaminoethyl methacrylate,
4 diethylaminoethyl methacrylate, diethylaminoethyl acrylamide, diethylaminoethyl
5 methacrylamide, diethylaminopropyl methacrylamide, aminopropyl acrylamide, 3-
6 (methacryloylamino)propyltrimethylammonium chloride, 2-aminoethyl methacrylate,
7 N-(3-aminopropyl)methacrylamide, 2-(t-butylamino)ethyl methacrylate, 2-(N, N-
8 dimethylamino)ethyl (meth)acrylate, N-(2-(N, N-dimethylamino))ethyl
9 (meth)acrylamide, N-(3-(N, N-dimethylamino))propyl methacrylamide, 2-
10 (meth)acryloyloxyethyltrimethylammonium chloride, 3-methacryloyloxy-2-

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11 hydroxypropyltrimethylammonium chloride, (2-acryloyloxyethyl)(4-
12 benzoylbenzyl)dimethylammonium bromide, 2-vinylpyridine, 4-vinylpyridine,
13 vinylimidazole, and derivatives thereof.

1 23. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a hydrophilic group and the hydrogel material is derived
3 from monomers selected from the group consisting of N-
4 (meth)acryloyltri(hydroxymethyl)methylamine, hydroxyethyl acrylamide,
5 hydroxypropyl methacrylamide, N-acrylamido-1-deoxysorbitol,
6 hydroxyethyl(meth)acrylate, hydroxypropylacrylate, hydroxyphenylmethacrylate,
7 polyethylene glycol monomethacrylate, polyethylene glycol dimethacrylate, acrylamide,
8 glycerol mono(meth)acrylate, 2-hydroxypropyl acrylate, 4-hydroxybutyl methacrylate, 2-
9 methacryloyloxyethyl glucoside, poly(ethyleneglycol) monomethyl ether monomethacrylate,
10 vinyl 4-hydroxybutyl ether, and derivatives thereof.

1 24. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a hydrophobic group and the hydrogel material is derived
3 from monomers selected from the group consisting of N, N-dimethyl acrylamide, N, N-
4 diethyl (meth)acrylamide, N-methyl methacrylamide, N-ethyl methacrylamide, N-propyl
5 acrylamide, N-butyl acrylamide, N-octyl (meth)acrylamide, N-dodecyl methacrylamide,
6 N-octadecyl acrylamide, propyl (meth)acrylate, decyl (meth)acrylate, stearyl
7 (meth)acrylate, octyl-triphenylmethylacrylamide, butyl-triphenylmethylacrylamide,
8 octadecyl-triphenylmethylacrylamide, phenyl-triphenylmethylacrylamide, benzyl-
9 triphenylmethylacrylamide, and derivatives thereof.

1 25. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a metal chelating group and the hydrogel material is
3 derived from monomers selected from the group consisting of N-(3-N, N-
4 bis(carboxymethylamino)propyl methacrylamide, 5-methacrylamido-2-(N, N-

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5 biscarboxymethylamino)pentanoic acid, N-(acrylamidoethyl)ethylenediamine N, N', N'-
6 triacetic acid, and derivatives thereof.

1 26. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a reactive group and the hydrogel material is derived from
3 monomers selected from the group consisting of glycidyl acrylate, acryloyl chloride,
4 glycidyl(meth)acrylate, (meth)acryloyl chloride, N-acryloxysuccinimide, vinyl azlactone,
5 acrylamidopropyl pyridyl disulfide, N-(acrylamidopropyl)maleimide, acrylamidodeoxy
6 sorbitol activated with bis-epoxirane compounds, allylchloroformate, (meth)acrylic
7 anhydride, acrolein, allylsuccinic anhydride, citraconic anhydride, allyl glycidyl ether,
8 and derivatives thereof.

1 27. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a thioether group and the hydrogel material is derived from
3 thiophilic monomers selected from the group consisting of 2-hydroxy-3-
4 mercaptopyridylpropyl (methacrylate), 2-(2-(3-
5 (meth)acryloxyethoxy)ethanesulfonyl)ethylsulfanyl ethanol, and derivatives thereof.

1 28. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a biotin group and the hydrogel material is derived from
3 biotin monomers selected from the group consisting of N-biotinyl-3-
4 (meth)acrylamidopropylamine and derivatives thereof.

1 29. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a boronate group and the hydrogel material is derived from
3 boronate monomers selected from the group consisting of N-(m-dihydroxyboryl)phenyl
4 (meth)acrylamide and derivatives thereof.

1 30. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a dye group and the hydrogel material is derived from dye

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3 monomers selected from the group consisting of N-(N'-dye coupled aminopropyl)
4 (meth)acrylamide and derivatives thereof.

1 31. (Once amended) The probe of claim 18 wherein the binding
2 functionalities [are] comprise a cholesterol group and the hydrogel material is derived
3 from cholesterol monomers selected from the group consisting of N-cholesteryl-3-
4 (meth)acrylamidopropylamine and derivatives thereof.

1 32. (Once amended) A probe that is removably insertable into a [gas
2 [phase ion] mass spectrometer, the probe comprising a substrate having a surface and a
3 plurality of particles that are substantially uniform in diameter on the surface, the
4 particles comprising binding functionalities for binding with an analyte detectable by the
5 mass spectrometer.

1 33. (As filed) The probe of claim 32 wherein the plurality of particles
2 have an average diameter of less than about 1000 μm .

1 34. (As filed) The probe of claim 32 wherein the particles have a
2 coefficient of diameter variation of less than about 5%.

1 35. (As filed) The probe of claim 32 wherein the surface of the
2 substrate is conditioned to adhere to the particles.

1 36. (As filed) The probe of claim 32 wherein the binding
2 functionalities of the particles are selected from the group consisting of a carboxyl group,
3 a sulfonate group, a phosphate group, an ammonium group, a hydrophilic group, a
4 hydrophobic group, a reactive group, a metal chelating group, a thioether group, a biotin
5 group, a boronate group, a dye group, a cholesterol group, and derivatives thereof.

1 37. (Cancel)

1 38. (Cancel)

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- 1 **39.** (Cancel)
- 1 **40.** (Cancel)
- 1 **41.** (Cancel)
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1 **75.** (Cancel)

1 **76.** (New) The probe of claim 1 wherein the binding functionality is a
2 reactive group selected from an epoxide and a carbonyldiimidazole.

1 **77.** (New) The probe of claim 1 wherein the hydrogel material is
2 derived from monomers selected from the group consisting of 3-
3 (methacryloylamino)propyltrimethylammonium chloride, 2-acrylamidoglycolic acid
4 and 5-methacrylamido-2-(N, N-biscarboxymethylamino)pentanoic acid.

1 **78.** (New) The probe of claim 1 wherein the hydrogel material
2 comprises cellulose or dextran.

1 **79.** (New) The probe of claim 1 wherein the surface is substantially
2 smooth.

1 **80.** (New) The probe of claim 1 wherein the hydrogel is about 1
2 micrometer thick.

1 **81.** (New) The probe of claim 1 wherein the substrate comprises an
2 insulating material.

1 **82.** (New) The probe of any of claims 1-4, 6-11, 13-31 or 76-81
2 wherein the surface of the substrate is conditioned with a coupling agent and the hydrogel
3 material adheres to the surface through a covalent interaction with the coupling agent.

1 **83.** (New) The probe of any of claims 1-4, 6-10, 14-31 or 76-81
2 wherein the hydrogel is attached to the surface in a plurality of discontinuous spots.

1 **84.** (New) The probe of claim 82 wherein the coupling agent is a
2 silane-based agent.

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1 85. (New) The probe of claim 82 wherein the hydrogel is attached to
2 the surface in a plurality of discontinuous spots.

1 86. (New) The probe of claim 1 wherein the binding functionality is a
2 reactive group selected from an epoxide and a carbonyldiimidazole.

1 87. (New) The probe of claim 32, 36 or 86 wherein the particles are
2 comprised of crosslinked polymers.

1 88. (New) The probe of claim 87 wherein the crosslinked polymers
2 comprise polystyrenes.

1 89. (New) The probe of claim 87 wherein the crosslinked polymers
2 comprise polysaccharides, agarose, dextran, methacrylates or functionalized silicon
3 dioxide.

1 90. (New) The probe of claim 87 wherein the particles comprise a
2 latex.

1 91. (New) The probe of claim 90 wherein the plurality of particles
2 have an average diameter of between about 0.1 μm to about 100 μm .

1 92. (New) The probe of claim 90 wherein the plurality of particles
2 have an average diameter of between about 1 μm to about 10 μm .

1 93. (New) The probe of claim 1 wherein the hydrogel material is less
2 than about one micrometer thick.

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CLAIMS PENDING AFTER AMENDMENT

1 1. (Once amended) A probe that is removably insertable into a mass
2 spectrometer, the probe comprising a substrate having a surface coated with silicon oxide
3 and a hydrogel material on the surface, wherein the hydrogel material is crosslinked and
4 comprises binding functionalities for binding with an analyte detectable by the mass
5 spectrometer.

1 2. (As filed) The probe of claim 1 wherein the substrate is in the
2 form of a strip or a plate.

1 3. (Once amended) The probe of claim 1 wherein the substrate
2 comprises an electrically conducting material.

1 4. (As filed) The probe of claim 1 wherein the surface of the
2 substrate is conditioned to adhere the hydrogel material.

1 6. (As filed) The probe of claim 1 wherein the surface of the
2 substrate is rough, porous or microporous.

1 7. (As filed) The probe of claim 1 wherein the hydrogel material is in
2 situ polymerized on the surface of the substrate.

1 8. (Once amended) The probe of claim 1 wherein the hydrogel
2 material is in situ polymerized on the silicon oxide coating by depositing a solution
3 comprising monomers onto the glass coating, wherein the monomers are pre-
4 functionalized to provide binding functionalities.

1 9. (Once amended) The probe of claim 1 wherein the thickness of the
2 coating and the hydrogel material combined is at least about 1 micrometer.

1 10. (As filed) The probe of claim 1 wherein the hydrogel material is at
2 least about 1 micrometer thick.

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1 11. (As filed) The probe of claim 1 wherein the hydrogel material is in
2 the form of a discontinuous pattern.

1 13. (As filed) The probe of claim 1 wherein the hydrogel material is
2 continuous and has one or two-dimensional gradient of one or more of the binding
3 functionalities.

1 14. (As filed) The probe of claim 1 wherein a plurality of different
2 hydrogel materials comprising different binding functionalities are on the surface of the
3 substrate.

1 15. (As filed) The probe of claim 1 wherein the hydrogel material is a
2 homopolymer, a copolymer, or a blended polymer.

1 16. (As filed) The probe of claim 1 wherein the hydrogel material is
2 derived from substituted acrylamide monomers, substituted acrylate monomers, or
3 derivatives thereof.

1 17. (As filed) The probe of claim 1 wherein the binding functionalities
2 attract the analyte by salt-promoted interactions, hydrophilic interactions, electrostatic
3 interactions, coordinate interactions, covalent interactions, enzyme site interactions,
4 reversible covalent interactions, nonreversible covalent interactions, glycoprotein
5 interactions, biospecific interactions, or combinations thereof.

1 18. (As filed) The probe of claim 1 wherein the binding functionalities
2 of the hydrogel material are selected from the group consisting of a carboxyl group, a
3 sulfonate group, a phosphate group, an ammonium group, a hydrophilic group, a
4 hydrophobic group, a reactive group, a metal chelating group, a thioether group, a biotin
5 group, a boronate group, a dye group, a cholesterol group, and derivatives thereof.

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1 19. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a carboxyl group and the hydrogel material is derived from
3 monomers selected from the group consisting of (meth)acrylic acid, 2-carboxyethyl
4 acrylate, N-acryloyl-amino hexanoic acid, N-carboxymethylacrylamide, 2-
5 acrylamidoglycolic acid, and derivatives thereof.

1 20. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a sulfonate group and the hydrogel material is derived from
3 acrylamidomethyl-propane sulfonic acid monomers or derivatives thereof.

1 21. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a phosphate group and the hydrogel material is derived from N-
3 phosphoethyl acrylamide monomers or derivatives thereof.

1 22. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise an ammonium group and the hydrogel material is derived from
3 monomers selected from the group consisting of trimethylaminoethyl methacrylate,
4 diethylaminoethyl methacrylate, diethylaminoethyl acrylamide, diethylaminoethyl
5 methacrylamide, diethylaminopropyl methacrylamide, aminopropyl acrylamide, 3-
6 (methacryloylamino)propyltrimethylammonium chloride, 2-aminoethyl methacrylate,
7 N-(3-aminopropyl)methacrylamide, 2-(t-butylamino)ethyl methacrylate, 2-(N, N-
8 dimethylamino)ethyl (meth)acrylate, N-(2-(N, N-dimethylamino))ethyl
9 (meth)acrylamide, N-(3-(N, N-dimethylamino))propyl methacrylamide, 2-
10 (meth)acryloyloxyethyltrimethylammonium chloride, 3-methacryloyloxy-2-
11 hydroxypropyltrimethylammonium chloride, (2-acryloyloxyethyl)(4-
12 benzoylbenzyl)dimethylammonium bromide, 2-vinylpyridine, 4-vinylpyridine,
13 vinylimidazole, and derivatives thereof.

1 23. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a hydrophilic group and the hydrogel material is derived from

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3 monomers selected from the group consisting of N-
4 (meth)acryloyltri(hydroxymethyl)methylamine, hydroxyethyl acrylamide,
5 hydroxypropyl methacrylamide, N-acrylamido-1-deoxysorbitol,
6 hydroxyethyl(meth)acrylate, hydroxypropylacrylate, hydroxyphenylmethacrylate,
7 polyethylene glycol monomethacrylate, polyethylene glycol dimethacrylate, acrylamide,
8 glycerol mono(meth)acrylate, 2-hydroxypropyl acrylate, 4-hydroxybutyl methacrylate, 2-
9 methacryloxyethyl glucoside, poly(ethyleneglycol) monomethyl ether monomethacrylate,
10 vinyl 4-hydroxybutyl ether, and derivatives thereof.

1 24. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a hydrophobic group and the hydrogel material is derived from
3 monomers selected from the group consisting of N, N-dimethyl acrylamide, N, N-diethyl
4 (meth)acrylamide, N-methyl methacrylamide, N-ethyl methacrylamide, N-propyl
5 acrylamide, N-butyl acrylamide, N-octyl (meth)acrylamide, N-dodecyl methacrylamide,
6 N-octadecyl acrylamide, propyl (meth)acrylate, decyl (meth)acrylate, stearyl
7 (meth)acrylate, octyl-triphenylmethylacrylamide, butyl-triphenylmethylacrylamide,
8 octadedcyl-triphenylmethylacrylamide, phenyl-triphenylmethylacrylamide, benzyl-
9 triphenylmethylacrylamide, and derivatives thereof.

1 25. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a metal chelating group and the hydrogel material is derived
3 from monomers selected from the group consisting of N-(3-N, N-
4 biscarboxymethylamino)propyl methacrylamide, 5-methacrylamido-2-(N, N-
5 biscarboxymethylamino)pentanoic acid, N-(acrylamidoethyl)ethylenediamine N, N', N'-
6 triacetic acid, and derivatives thereof.

1 26. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a reactive group and the hydrogel material is derived from
3 monomers selected from the group consisting of glycidyl acrylate, acryloyl chloride,
4 glycidyl(meth)acrylate, (meth)acryloyl chloride, N-acryloxysuccinimide, vinyl azlactone,

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5 acrylamidopropyl pyridyl disulfide, N-(acrylamidopropyl)maleimide, acrylamidodeoxy
6 sorbitol activated with bis-epoxirane compounds, allylchloroformate, (meth)acrylic
7 anhydride, acrolein, allylsuccinic anhydride, citraconic anhydride, allyl glycidyl ether,
8 and derivatives thereof.

1 27. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a thioether group and the hydrogel material is derived from
3 thiophilic monomers selected from the group consisting of 2-hydroxy-3-
4 mercaptopyridylpropyl (methacrylate), 2-(2-(3-
5 (meth)acryloxyethoxy)ethanesulfonyl)ethylsulfanyl ethanol, and derivatives thereof.

1 28. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a biotin group and the hydrogel material is derived from biotin
3 monomers selected from the group consisting of N-biotinyl-3-
4 (meth)acrylamidopropylamine and derivatives thereof.

1 29. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a boronate group and the hydrogel material is derived from
3 boronate monomers selected from the group consisting of N-(m-dihydroxyboryl)phenyl
4 (meth)acrylamide and derivatives thereof.

1 30. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a dye group and the hydrogel material is derived from dye
3 monomers selected from the group consisting of N-(N'-dye coupled aminopropyl)
4 (meth)acrylamide and derivatives thereof.

1 31. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a cholesterol group and the hydrogel material is derived from
3 cholesterol monomers selected from the group consisting of N-cholesteryl-3-
4 (meth)acrylamidopropylamine and derivatives thereof.

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1 32. (Once amended) A probe that is removably insertable into a mass
2 spectrometer, the probe comprising a substrate having a surface and a plurality of
3 particles that are substantially uniform in diameter on the surface, the particles
4 comprising binding functionalities for binding with an analyte detectable by the mass
5 spectrometer.

1 33. (As filed) The probe of claim 32 wherein the plurality of particles
2 have an average diameter of less than about 1000 μm .

1 34. (As filed) The probe of claim 32 wherein the particles have a
2 coefficient of diameter variation of less than about 5%.

1 35. (As filed) The probe of claim 32 wherein the surface of the
2 substrate is conditioned to adhere to the particles.

1 36. (As filed) The probe of claim 32 wherein the binding
2 functionalities of the particles are selected from the group consisting of a carboxyl group,
3 a sulfonate group, a phosphate group, an ammonium group, a hydrophilic group, a
4 hydrophobic group, a reactive group, a metal chelating group, a thioether group, a biotin
5 group, a boronate group, a dye group, a cholesterol group, and derivatives thereof.

1 76. (New) The probe of claim 1 wherein the binding functionality is a
2 reactive group selected from an epoxide and a carbonyldiimidazole.

1 77. (New) The probe of claim 1 wherein the hydrogel material is
2 derived from monomers selected from the group consisting of 3-
3 (methacryloylamino)propyltrimethylammonium chloride, 2-acrylamidoglycolic acid
4 and 5-methacrylamido-2-(N, N-biscarboxymethylamino)pentanoic acid.

1 78. (New) The probe of claim 1 wherein the hydrogel material
2 comprises cellulose or dextran.

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1 **79.** (New) The probe of claim 1 wherein the surface is substantially
2 smooth.

1 **80.** (New) The probe of claim 1 wherein the hydrogel is about 1
2 micrometer thick.

1 **81.** (New) The probe of claim 1 wherein the substrate comprises an
2 insulating material.

1 **82.** (New) The probe of any of claims 1-4, 6-11, 13-31 or 76-81
2 wherein the surface of the substrate is conditioned with a coupling agent and the hydrogel
3 material adheres to the surface through a covalent interaction with the coupling agent.

1 **83.** (New) The probe of any of claims 1-4, 6-10, 14-31 or 76-81
2 wherein the hydrogel is attached to the surface in a plurality of discontinuous spots.

1 **84.** (New) The probe of claim 82 wherein the coupling agent is a
2 silane-based agent.

1 **85.** (New) The probe of claim 82 wherein the hydrogel is attached to
2 the surface in a plurality of discontinuous spots.

1 **86.** (New) The probe of claim 1 wherein the binding functionality is a
2 reactive group selected from an epoxide and a carbonyldiimidazole.

1 **87.** (New) The probe of claim 32, 36 or 86 wherein the particles are
2 comprised of crosslinked polymers.

1 **88.** (New) The probe of claim 87 wherein the crosslinked polymers
2 comprise polystyrenes.

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1 **89.** (New) The probe of claim 87 wherein the crosslinked polymers
2 comprise polysaccharides, agarose, dextran, methacrylates or functionalized silicon
3 dioxide.

1 **90.** (New) The probe of claim 87 wherein the particles comprise a
2 latex.

1 **91.** (New) The probe of claim 90 wherein the plurality of particles
2 have an average diameter of between about 0.1 μm to about 100 μm .

1 **92.** (New) The probe of claim 90 wherein the plurality of particles
2 have an average diameter of between about 1 μm to about 10 μm .

1 **93.** (New) The probe of claim 1 wherein the hydrogel material is less
2 than about one micrometer thick.

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